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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/380,682	10/19/99	MOSSAKOWSKA	D 88362/107

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EXAMINER	
BRANNOCK, M	
ART UNIT	**PAPER NUMBER**
1646	18

DATE MAILED: 11/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/380,682	Mossakowska
Examiner	**Art Unit**
Michael Brannock, Ph.D.	1646

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 24, 2001*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *28-51* is/are pending in the applica

4a) Of the above, claim(s) *30-41, 44-48, and 51* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *28, 29, 42, 43, 49, and 50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Status of Application: Claims and Amendments

1. Claims 28-51 are pending.

2. Claims 30-41, 44-48 and 51 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, as discussed previously in Paper 14, 2/28/01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 28, 29 42, 43, 49 and 50 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons set forth in paragraphs a-d, g and j of item 5 of Paper 14, reiterated and discussed below:

a) The claims require a polypeptide comprising short consensus repeats "as the only structurally and functionally intact SCR domains of CR1". This phrase is confusing and renders the claims indefinite for several reasons. First, it is unclear what relationship CR1 has to the claimed polypeptide, e.g. *is* the claimed polypeptide CR1 or an example of CR1 or different than CR1? Is this phrase meant to be an aside or a parenthetical statement describing CR1, but not placing any limitations on the claimed polypeptide? Second, the specification has not provided

sufficient guidance to one of skill in the art to be able to unambiguously conclude what is and what is not a structurally and functionally intact SCR domain - such determination being required to establish the bounds of the claim. The description of the term "SCR" at pages 1-2 of the specification is insufficient to allow one of skill in the art to be able to unambiguously conclude what is and what is not a "structurally and functionally intact SCR domain". Further, the words "structurally" and "functionally" are relative words and it is impossible to know what is and what is not encompassed by these terms as they are used in the claims.

Applicant convincingly argues that the term "SCR" is well known in the art and that the skilled artisan would understand what is and what is not an "SCR"; however, as set forth previously, the phrase "as the only structurally and functionally intact SCR domains of CR1" renders the claims in definite. As set forth above, it is not clear what limitations are placed on the *claimed* polypeptides because this phrase appears to refer to CR1 and not to the claimed polypeptides. Applicant argues that this phrase means that the polypeptide comprises one to four SCRs and that these SCRs are structurally and functionally similar to those in the native wild type receptor. This argument has been fully considered but not deemed persuasive. The claims, as written, do not require what Applicant suggests and simply do not make sense syntactically. Further, it is unclear how (or how much) the SCRs of the claims are required to be structurally or functionally similar to those of the native wildtype, as is suggested by Applicant. As set forth previously the words "structurally" and "functionally" are relative words and it is impossible to know what is and what is not encompassed by these terms as they are used in the claims.

b) The phrase "wherein at least one of the native amino acids is substituted" (e.g. claim 28) is indefinite because the claims do not set forth which polypeptide, nor which portion thereof, is considered "native".

In response "Applicants point out that the native amino acids refer to the SCRs comprising the polypeptide as described in the claim". This argument has been fully considered but not deemed persuasive. First, the claim does not indicate that a particular SCR comprises any polypeptide, as is asserted by Applicant. The claims do not set forth which polypeptide, nor which amino acid sequence, is "native". The claim language is ambiguous as to which part, or parts, of the claim the phrase "wherein at least one of the native amino acids is substituted" is meant to refer to.

c) The positions of the proposed amino acid substitutions are indefinite (e.g. Val at position 4, claim 28) because the claim does not put forth where the numbering is to start from, e.g. is this position 4 of the claimed polypeptide, or of CR1 or of LHR-A or of any one of the SCR domains? Applicant argues that the substitutions are in relation to the native CR1 sequence starting at SCR1. This argument has been fully considered but not deemed persuasive because the claims do not set forth what reference point the numbering begins and nor could such a reference pointed be unambiguously inferred from either the claims or the specification.

d) Claims 42, 43 and 49 require "derivatives" of the recited polypeptide. The word "derivatives" renders the claims indefinite because the claims include amino acid sequences and chemical modification not actually disclosed, thereby rendering the metes and bounds of the

claim unascertainable. The specification provides some examples of derivatives, however, examples are not sufficient to define the bounds of a claim. The specification does not provide guidelines for measuring the degree of "derivation" nor can the metes and bounds of the term "derivative" be ascertained when read in light of the specification. One of ordinary skill in the art, would not be reasonably apprised of the metes and bounds of the invention.

Applicant argues that the derivatives are the polypeptides comprising SCRs, well known in the art, as set forth in SEQ ID NO: 1, with at least one of the listed substitutions. This argument has been fully considered but not deemed persuasive for the reasons given above.

g) In claim 42 the term "thermodynamic additivity" renders the claim indefinite because there is no art-recognized definition of the term and nor is the description of the term at page 8 of the specification sufficient to allow one of skill in the art to be able to unambiguously conclude what is and what is not ""thermodynamic additivity". Applicant argues that this term has been well known to one skilled in the art and has been in practice. Applicant points to Murphy and Gill. et al. page 699, paragraph 1, lines 1-4, in support of this assertion. This argument has been fully considered but not deemed persuasive; this term does not appear to be used by Murphy and Gill.

j) It is suggested to Applicant that sequence identifiers, of the form SEQ ID NO: X, be used in the claims such that the metes and bounds of the claims can be ascertained.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 43 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polypeptide of SEQ ID NO: 1, yet the claim encompasses polypeptide derivatives not described in the specification, i.e. those comprising membrane binding sequences identified through screening of random chemical libraries. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the positions or identities of those sequences based on the information disclosed in the specification.

With the exception of the of the polypeptide of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants. Therefore, only the polypeptide of SEQ ID NO: 1, and polypeptides derivatives thereof comprising membrane binding elements taught in the specification, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant asserts that the examiner has not satisfied the guidelines for making a rejection for lack of written description, however no specific arguments have been set forth to support the

assertion. Applicant further argues that the specification describes derivatives of membrane binding sequences in addition to SEQ ID NO: 1 at page 10 of the specification. This argument has been fully considered but not deemed persuasive. There appears to be no description of any polypeptides comprising membrane binding sequences identified through screening of random chemical libraries, as is required by the claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 28, 29, and 50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5545619 in view of Hourcade et al., J. Biol. Chem. 265(2)974-980, 1990, as set forth in item 9 of Paper 14, and reiterated below.

U.S. Patent No: 5545619 teaches a soluble polypeptide (CR1) comprising one to four short consensus repeats of the long homologous repeat A (LHR-A) and related polypeptides termed RCA polypeptides (see col 6), methods of producing mutations is said polypeptides (see col 7), and pharmaceutical compositions containing therapeutically effective amounts of same (see col. 9). By way of reference to Hourcade et al., U.S. Patent No: 5545619 discloses that amino acid sequences having the mutations recited in the instant claims are encompassed by the

invention (see col. 6, lines 6-15). These mutations are disclosed by Hourcade et al., (see Figure 3), as pointed to by U.S. Patent No: 5545619. Claim 42 also requires that the polypeptide derivative comprises at least two heterologous membrane binding elements with low membrane affinity, covalently associated with the polypeptide, wherein the elements are capable of interacting independently and with thermodynamic additivity with the components of cellular membranes exposed to extracelluar fluids. The instant specification states that preferred membrane binding elements are basic amino acid sequences (see the bottom of page 9). The amino acid sequence taught by Hourcade et al. provides for at least 8 heterologous basic amino acids (arginine and lysine) relative to CR1 (see Figure 3 of Hourcade et al.).

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, with reasonable expectation of success, to produce a polypeptide having the amino acid sequence taught by Hourcade et al. when practicing the invention disclosed in U.S. Patent No: 5545619. The motivation to do so was provided in U.S. Patent No: 5545619 wherein it was stated that the term "RCA proteins" refers to that taught by Hourcade et al. (see col. 6, lines 6-15), and that such proteins are useful in therapeutic and prophylactic contexts (see the last paragraph of col. 8).

Applicant argues that "the present invention is relevant to non-obvious mutations in CR1 including "SCR3" which is not in the teachings of U.S. Patent No: 5545619 nor Hourcade et al.". This argument has been fully considered but not deemed persuasive. First, no claims *require* that the mutations be in SCR3. Never-the-less, U.S. Patent No: 5545619 teaches that the mutations

disclosed by Hourcade et al. are encompassed by the invention of U.S. Patent No: 5545619 (see col. 6, lines 6-15). Hourcade et al. disclose the mutations recited in the claims (wherein the numbering begins at SCR1, see Fig 3) which include mutations in SCR3, see Fig 3.

Applicant argues that U.S. Patent No: 5545619 in combination with Hourcade et al. concerns CR1 diversity rather than purposeful mutation and substitutions as disclosed in the instant Application. This argument has been fully considered but not deemed persuasive. U.S. Patent No: 5545619 clearly teach that the polypeptides be purposely modified and amino acid sequences be substituted among the known sequences of RCA protein sequences - including those of Hourcade et al., see col 6.

Applicant further argues that it was believed at the time the invention was made that mutation in SCR3 would result in inactive polypeptide. This argument has been fully considered but not deemed persuasive. Again, the claims do not require every embodiment of the claimed invention have mutations in SCR3. Second, U.S. Patent No: 5545619 do not indicate that the mutation in SCR3 disclosed by Hourcade et al. would not be expected to work. Third, Applicant has any provided no evidence that one of skill in the art would have doubted the teachings of U.S. Patent No: 5545619.

Applicant again argues that U.S. Patent No: 5545619 does not teach mutation and that Hourcade et al. describes natural substitutions in CR1, which does not describe or provide indication to any of the purposeful substitutions in SCR3 as described in the instant application and recited in the claims. This argument has been fully considered but not deemed persuasive.

U.S. Patent No: 5545619 clearly teach that the polypeptides be purposely modified and amino acid sequences be substituted among the known sequences of RCA protein sequences - including those of Hourcade et al., see col 6. The substitutions described by Hourcade et al. are recited in the instant claims. Further, as indicated above, the claims do not require mutations in SCR3, only that the polypeptide "include at least SCR3".

9. Claims 43 and 49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5545619 in view of Hourcade et al., J. Biol. Chem. 265(2)974-980, 1990, as applied to claims 28, 29, 42 and 50 above, and in further view of Clissold et al., Eur. J. Immunol., 23(2346-2352)1993 and U.S. Patent No: 5936092, as set forth previously in item 10 of Paper 14.

As now amended, claim 43 does not claim the soluble derivative of claim 42, but instead claims the soluble polypeptide of claim 42. Never-the-less, claim 43 is still encompassed by the instant rejection. As set forth previously, claims 43 and 49 contain the elements discussed above regarding claims 28, 29, 42 and 50, yet claims 43 and 49 also recite that the polypeptide comprise at least two heterologous membrane binding elements consisting of fatty acid derivatives. Claim 49 also requires that the process of constructing the polypeptide include recovering the polypeptide and, thereafter, post-transnationally modifying the polypeptide to chemically introduce the membrane binding elements.

Clissold et al. teach that the addition of a membrane binding element (glycosyl-phosphatidylinositol, GPI) to soluble CR1 increases the effectiveness of CR1 at protecting cells

from complement mediated damage (see the abstract). Thus, Clissold et al. teach the concept that membrane binding elements increase the effectiveness of CR1. In the experiments of Clissold et al., there is only a single membrane binding element, and that element was added to CR1 during the expression of the polypeptide and not after recovery, as required by claim 49. However, the conjugation of fatty acid molecules to proteins for use in directing the proteins to the membrane of cells is well known in the art. U.S. Patent No: 5936092 discloses methods of conjugating fatty acid moieties to polypeptides for after the polypeptides have been expressed and recovered (see, for example, col. 10)

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to post-transnationally modify a polypeptide, said polypeptide being taught by Patent No: 5545619 in view of Hourcade et al., as discussed above, with membrane binding elements using the methods disclosed by U.S. Patent No: 5936092. The motivation to do so was provided by Clissold et al. who teach the concept that membrane binding elements increase the effectiveness of CR1.

Applicants arguments are based on the applicability of U.S. Patent No: 5545619 in view of Hourcade et al.. These arguments have been fully considered and fully addressed above.

New Rejections:

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claim 43 is rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No: 5936092.

As now amended claim 43 does not claim the soluble derivative of claim 42, but instead claims the soluble polypeptide of claim 42. Therefore claim 43 requires any soluble polypeptide which comprises at least two heterologous membrane binding elements consisting of fatty acid derivatives. U.S. Patent No: 5936092 discloses a hydrophilic polypeptide (i.e. soluble) conjugated with at least four fatty acid derivatives (see cols. 10-11).

Conclusion

12. No claims are allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Fridays from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler

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October 29, 2001